



2003-2004 Influenza Vaccine Efficacy at Fort Lee, Virginia

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Abstract:

In November 2003, Fort Lee, Virginia experienced an influenza outbreak in the 23rd Quartermaster Advanced Individual Training (AIT) Brigade. Post medical personnel responded by implementing both isolation and mass immunization measures. Due to the early onset of the 2003-2004 influenza season and the introduction of an unanticipated H3N2 Fujian strain, an Epidemiological Consult team from USACHPPM, WRAIR, and AFIOH launched an investigation to determine the efficacy of the current influenza vaccine. Attack rates among two vaccine cohorts (immunized vs. unimmunized) were determined based on loose and tight case definitions to evaluate vaccine efficacy; and adjunct survival analysis was performed. An overview of the outbreak and findings from this investigation will be presented.

Introduction:

Respiratory diseases such as influenza have a long history of associated morbidity and mortality both at global and local levels. Military trainees are particularly vulnerable to outbreaks because they live and train under stressful, crowded conditions. The most notorious of the influenza outbreaks, the pandemic of 1918-9 which was responsible for the death of over 21 million people worldwide, began at a military training post (Camp Funston, Kansas). To date there have been 7 confirmed influenza pandemics and due to the variable nature of circulating influenza strains there is an ever-present threat of future pandemics.

Because annual influenza vaccination is currently the best defense against the disease it is important to closely monitor both disease occurrence and immunization status in order to determine the effectiveness of available vaccines. The recent influenza outbreak at Ft. Lee, VA, occurring on the heels of an early influenza season and introduction of a viral strain not closely matched by the vaccine, prompted such an assessment.

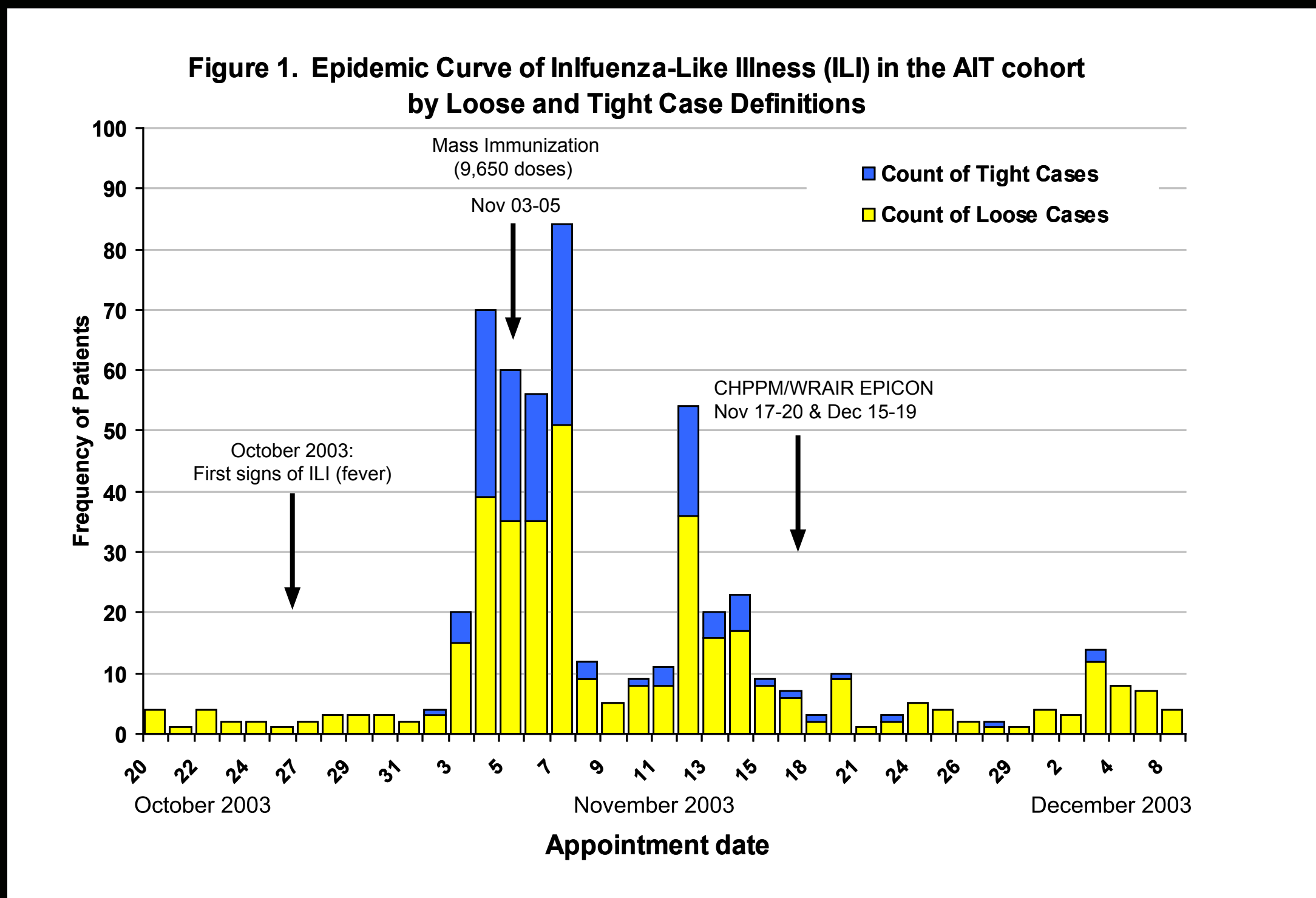
Background: Influenza Outbreak, 11/03-12/03, Fort Lee, Virginia

Population:

- US Army Advanced Individual Training Brigade of approximately 3000 young soldiers in close proximity for training at any given time
- Dynamic population training for 6 to 12 weeks depending on military occupational specialty (MOS) with weekly arrivals and departures
- Modern dormitory-style housing with 3 to 4 trainees per room
- Three battalions: 10 company sized units with 200-400 trainees each
- Significant mixing during meals (up to 1,200 trainees fed in a 90-minute period at three dining facilities)

Timeline (Figure 1):

- Early 11/03 influenza outbreak: virologic confirmation of H3N2 Fujian Strain
- Influenza vaccine mass immunization as control measure initiated 11/03/2003
- Epidemiologic consults initiated 11/17/2003 and 12/15/2003



Methods: Data Collection and Analysis:

- A consolidated database was compiled to include medical, immunization, and personnel records for the 23rd Quartermaster brigade AIT population from 10/31/2003 – 12/15/2003. Data sources included: MEDPROS, ESSENCE, medical records and personnel rosters from Epi-Consultation)
- Person time contributed by each AIT participant within the observation period was determined based on personnel data which included arrival/departure dates and MOS. When missing either arrival or departure data, MOS (which determines length of training) was used to estimate the missing date.
- Immune time was calculated based on a conservative 14-day interval for the influenza vaccine to become effective; time spent unvaccinated or prior to the completion of the 14 days post vaccination was considered non-immune time. Therefore, each AIT participant contributed immune and/or non-immune time during the observation period (i.e. partial immunity).
- Based on immune status, two cohorts were constructed: immune vs non-immune. Attack rates were calculated for each group based on both a loose and tight case definition.
- Using the derived measures, estimates of vaccine efficacy within 95% confidence intervals were calculated.
- Survival analysis (Kaplan-Meier, log rank test) was performed to further evaluate significant differences in time to event data between the vaccine cohorts.

Case Definitions:

Loose	Tight
Primary Diagnosis of ILI	Primary Diagnosis of ILI Fever (>100.5) AND Respiratory Symptoms (e.g. cough or sore throat)

*Primary diagnosis of ILI based on ESSENCE syndromic groups
** Influenza laboratory confirmation available for small fraction of ILI cases; 30/59 isolates (50.8%) tested positive for influenza. Antigenic characterization not performed.

Vaccine Efficacy (VE) Calculations:

Vaccine Efficacy:

Vaccine Efficacy (VE) = 1 – relative risk (RR)

RR = attack rate in immunized / attack rate in unimmunized

95% Confidence Interval (CI):

95% CI = $\text{Exp}[\ln(\text{RR}^a) \pm 1.96 \times \text{SD}[\ln(\text{RR}^a)]]$

$\text{SD}[\ln(\text{RR}^a)] = \sqrt{1/a + 1/b}$

Where a=#cases in immunized group &
b=#cases in unimmunized group

Results:

- The majority of the AIT cohort were white, male, and less than 20 years of age [Table 1].
- Less than half of the AIT cohort were vaccinated with the 2003-2004 influenza vaccine during the observation window (10/31/2003 – 12/15/2003) [Table 2].
- Most vaccinated soldiers were only partially immunized, contributing both immune and non-immune person time during the observation period [Table 2].
- Calculated vaccine efficacy estimates in Tables 3 & 4 show a positive vaccine response in those who were vaccinated compared to those who were not vaccinated.
- Figures 5 & 6 show a small but significant increase in survival time among the vaccinated cohort which further highlights the effectiveness of the vaccine.

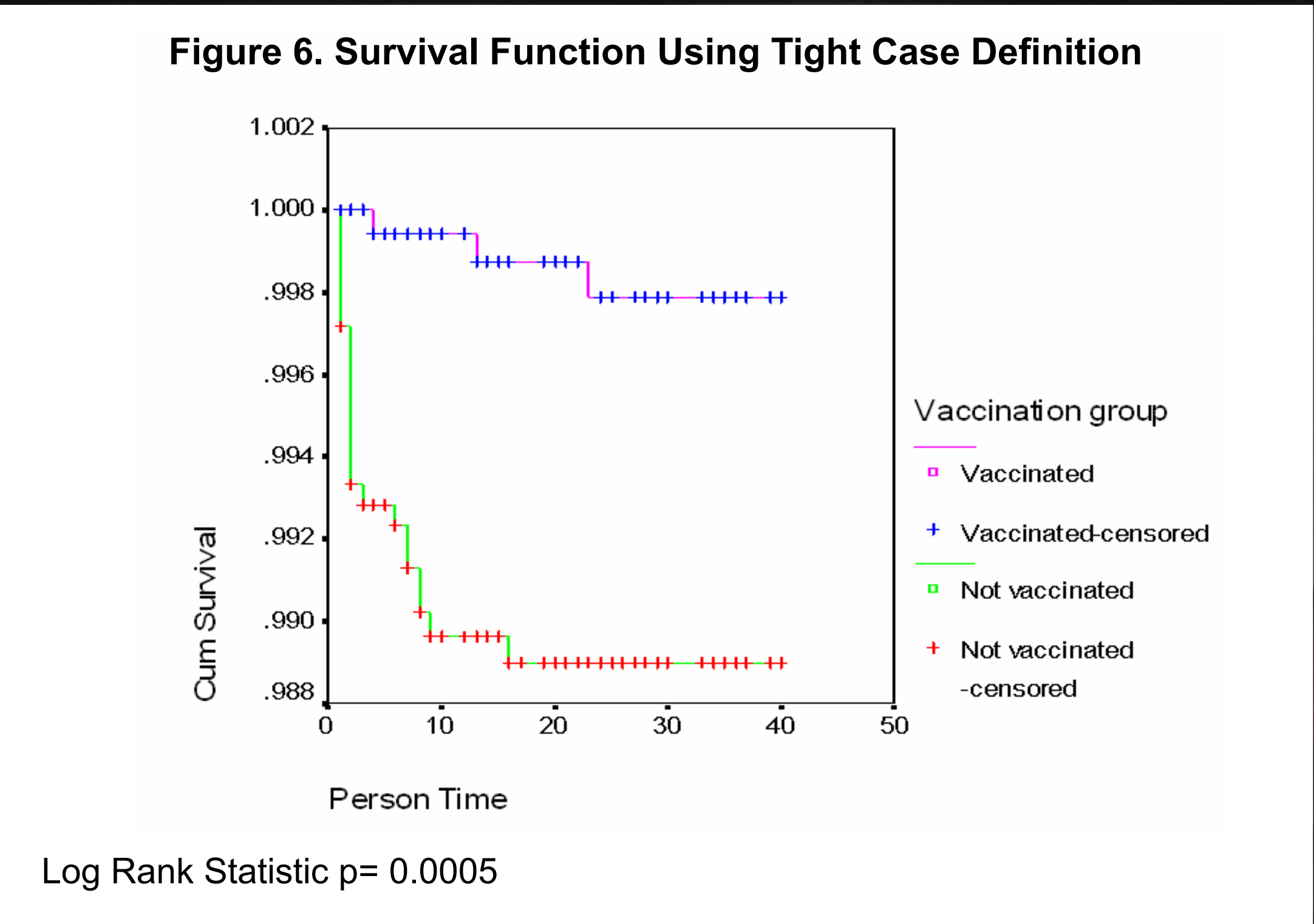
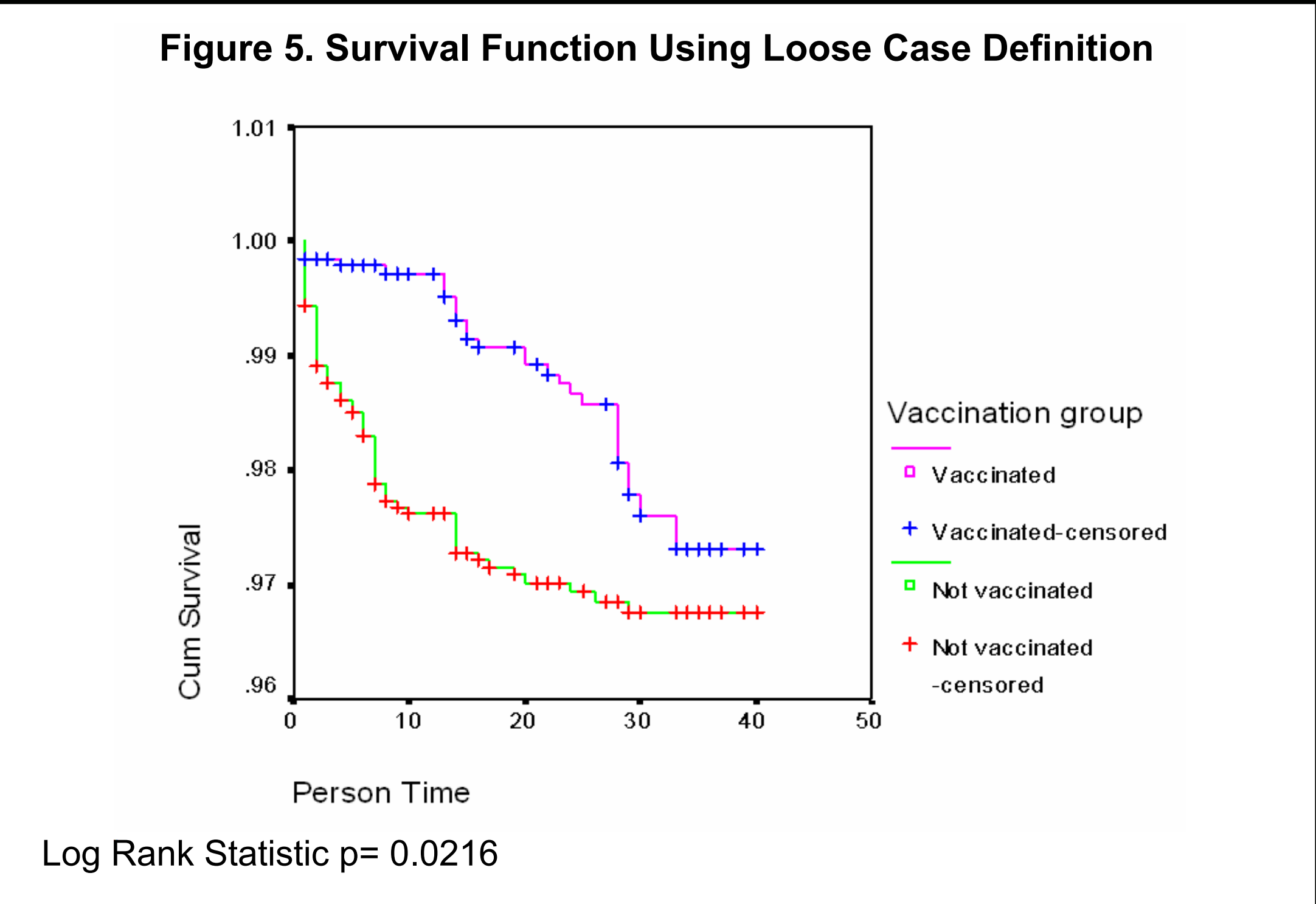
Table 1. Demographics for AIT Cohort (10/31/03-12/15/03)			
Variable	Variable Description	n	Proportion in Category (%)
Age	<20 years	2305	55.7%
	20-24 years	1369	33.1%
	25-29 years	281	6.8%
	>30 Years	186	4.5%
	Total	4141	100
Ethnicity	White, non-Hispanic	2529	58.8%
	Black, non-Hispanic	1226	28.5%
	Other	545	12.6%
	Total	4300	100
Sex	Male	2730	65.9%
	Female	1411	34.1 %
	Total	4141	100

Table 2. Immunization status of AIT Cohort (10/31/2003 – 12/15/2003)			
Variable	Variable Description*	n	Proportion in Category (%)
Case - Loose Definition (n=388)	Full-immunity	10	2.6
	Partial immunity	19	5.0
	No immunity	352	92.4
Case – Tight Definition (n=159)	Full-immunity	1	0.6
	Partial immunity	1	0.6
	No immunity	155	98.7
NonCases (n=3912)	Full-immunity	487	12.6
	Partial immunity	1199	31.2
	No immunity	2156	56.2

* Immune status unknown for a small fraction of the cohort

Table 3. Vaccine Efficacy (VE) Results: Loose Case Definition			
	Disease + counts	Person-time	Attack Rate
Immune +	29	42188 person-days	0.0006874
Immune -	352	90709 person-days	0.00388054
RR = 0.17714 VE = 82.3% (CI:43.7-94.4%)			

Table 4. Vaccine Efficacy (VE) Results: Tight Case Definition			
	Disease + counts	Person-time	Attack Rate
Immune +	2	42188 person-days	0.000047407
Immune -	155	90709 person-days	0.0017088
RR = 0.027743 VE = 97.2% (88.8-99.3%)			



Limitations:

- Vaccine efficacy against influenza and specific circulating viral antigens such as the H3N2/Fujian strain cannot be demonstrated due to the scarcity of the Influenza isolates collected; therefore, results are limited to the vaccine's overall effectiveness in preventing ILI and probable influenza.
- Use of non-specific ILI case definitions may underestimate vaccine effectiveness.
- The conservative use of a 14 day post vaccination window to determine immunization status may have also underestimated vaccine effectiveness.
- Early influenza activity in relation to timing of receiving vaccination complicated analysis.
- Timely and pertinent data extraction proved difficult to obtain at the local level; supplemental data from outside sources greatly enhanced analysis, but took a considerable amount of time to capture.

Conclusion:

Annual fluctuations in circulating influenza viral strains necessitate vigilant influenza surveillance and vaccine development. The early onset of the 2003-2004 flu season, coupled with the introduction of an unanticipated viral strain, served to heighten awareness of the importance of supplementing surveillance and preventive vaccine efforts with rapid assessment of vaccine efficacy. Findings from the Ft. Lee vaccine efficacy study indicate that the 2003-2004 influenza vaccine was effective against ILI and probable influenza among the AIT cohort. Future studies could be greatly enhanced through increased influenza laboratory confirmation and improved data capture coordination/consolidation efforts.

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- Contribution of military immunization data (MEDPROS)
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